A regenerative approach to the treatment of multiple sclerosis.

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Authors: Vishal A Deshmukh, Virginie Tardif, Costas A Lyssiotis, Chelsea C Green, Bilal Kerman, Hyung Joon Kim, Krishnan Padmanabhan, Jonathan G Swoboda, Insha Ahmad, Toru Kondo, Fred H Gage, Argyrios N Theofilopoulos, Brian R Lawson, Peter G Schultz, Luke L Lairson

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Public Summary:
Progressive phases of multiple sclerosis are associated with inhibited differentiation of the progenitor cell population that generates the mature oligodendrocytes required for remyelination and disease remission. To identify selective inducers of oligodendrocyte differentiation, we performed an image-based screen for myelin basic protein (MBP) expression using primary rat optic-nerve-derived progenitor cells. Here we show that among the most effective compounds identifed was benztropine, which significantly decreases clinical severity in the experimental autoimmune encephalomyelitis (EAE) model of relapsing-remitting multiple sclerosis when administered alone or in combination with approved immunosuppressive treatments for multiple sclerosis. Evidence from a cuprizone-induced model of demyelination, in vitro and in vivo T-cell assays and EAE adoptive transfer experiments indicated that the observed efficacy of this drug results directly from an enhancement of remyelination rather than immune suppression. Pharmacological studies indicate that benztropine functions by a mechanism that involves direct antagonism of M1 and/or M3 muscarinic receptors. These studies should facilitate the development of effective new therapies for the treatment of multiple sclerosis that complement established immunosuppressive approaches.

Scientific Abstract:
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